

Application No.: 09/828,607  
Amendment dated March 23, 2004  
In response to Examiner's Office Action dated December 23, 2003

**REMARKS**

Claims 1-27, 30-34, 47, 48, 50 and 57-60 are pending in this application.

Applicants have cancelled claims 28 and 49 without prejudice, and reserve their right to prosecute the subject matter of the cancelled claims in any future application claiming benefit or priority herefrom under 35 U.S.C. § 120.

Applicants have amended claims 1 and 47 to recite methods for repairing a defect locus in a nonarticular cartilage tissue and promoting chondrogenesis at a nonarticular defect locus, respectively, comprising the steps of a) preparing an osteogenic protein comprising an osteogenic protein disposed in a carrier, wherein the osteogenic protein is selected from the group consisting of OP-1, OP-2, OP-3, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-9, BMP-10, BMP-11, BMP-15, BMP-3B, DPP, Vg-1, Vgr-1, 60A protein, GDF-1, GDF-2, GDF-3, GDF-8, GDF-9, GDF-10 and GDF-11; and b) implanting the osteogenic device into the defect locus, thereby inducing the formation of functional cartilage

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tissue. Support for this amendment is provided, for example, at specification page 3, lines 9-11; page 4, lines 12-24 and in claims 1, 26, 27, 47 and 50 as originally filed.

Applicants have amended claim 27 to properly depend from amended claim 1.

None of the amendments adds new matter.

Applicants address the Examiner's rejection below:

**35 U.S.C. § 132**

The Examiner has objected to applicants' amendments filed September 8, 2003 under 35 U.S.C. § 132 stating that the amendment introduces new matter into the disclosure of the invention. Specifically, the Examiner asserts that there is no support in the original specification for the negative proviso that the osteogenic protein of SEQ ID NO: 6 may not be GDF-5 or GDF-6. The Examiner states that cancellation of the new matter is required.

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Applicants have amended the claims to delete the negative proviso language and to recite specific osteogenic proteins. Accordingly, the Examiner's objection has been obviated.

**35 U.S.C. § 112, 1st Paragraph**

Claims 1-28, 30-34, 47-50 and 57-60

The Examiner has rejected claims 1-28, 30-34, 47-50 and 57-60 under 35 U.S.C. § 112, first paragraph, for lack of written description. The Examiner contends that the claims recite added material which is not supported by the original disclosure. Specifically, the Examiner asserts that the negative proviso that the osteogenic protein of SEQ ID NO: 6 may not be GDF-5 or GDF-6 is not supported in the instant specification.

As described above, applicants have amended claims 1 and 47 (and therefore, claims dependent thereon) to cancel recitation of the proviso. Accordingly, applicants request that the Examiner withdraw this written description rejection.

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**35 U.S.C. § 112, 2nd Paragraph**

Claims 1-28, 30-34, 47-50 and 57-60

The Examiner has rejected claims 1-28, 30-34, 47-50 and 57-60 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner contends that claims 1 and 47, and the claims dependent thereon, are unclear as to what is intended by the recitation of "administering an osteogenic device" because it is unclear how to administer a device as the word "administer" means to manage or dispense.

Applicants have amended claims 1 and 47 (and therefore, the claims dependent thereon) to recite that the methods comprise the steps of a) preparing an osteogenic device comprising an osteogenic protein disposed in a carrier, wherein the osteogenic protein is selected from the group consisting of OP-1, OP-2, OP-3, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-9, BMP-10, BMP-11, BMP-15, BMP-3B, DPP, Vg-1, Vgr-1, 60A protein, GDF-1, GDF-2, GDF-3, GDF-8, GDF-9, GDF-10 and GDF-11; and b) implanting the

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osteogenic device into the defect locus, thereby inducing the formation of functional replacement cartilage tissue. Applicants respectfully submit that the claims, as amended, obviate the indefiniteness rejection.

**35 U.S.C. § 102(b)**

Claims 1-4, 7-11, 14-16, 25, 27, 47, 48, 57, 59 and 60

The Examiner has rejected claims 1-4, 7-11, 14-16, 25, 27, 47, 48, 57, 59 and 60 under 35 U.S.C. § 102(b) as being anticipated by WO 96/14335 ("Luyten"). The Examiner asserts that Luyten discloses that CDMP-1 and CDMP-2 have *in vivo* chondrogenic activity in combination with a matrix for the repair of cartilage. The Examiner further states that Luyten teaches that the CDMPs can be combined with a number of suitable carriers and that the formulation can be administered via an injection.

Applicants have amended claims 1 and 47 (and therefore, claims dependent thereon) to recite that the osteogenic protein is selected from the group consisting of OP-1, OP-2, OP-3, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-9, BMP-10, BMP-11, BMP-15,

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BMP-3B, DPP, Vg-1, Vgr-1, 60A protein, GDF-1, GDF-2, GDF-3, GDF-8, GDF-9, GDF-10 and GDF-11. Luyten discloses the use of CDMP-1 and CDMP-2 for stimulating chondrogenic activity without substantially stimulating osteogenic activity. Luyten does not disclose the use of any of the osteogenic proteins recited in the amended claims for repairing nonarticular cartilage tissue or promoting chondrogenesis at a nonarticular defect locus. Accordingly, applicants respectfully request that the Examiner withdraw this novelty rejection.

**35 U.S.C. § 103(a)**

Claims 1-6, 7-25, 27, 30-34, 47, 48, 57 and 59-60

The Examiner has rejected claims 1-6, 7-25, 27, 30-34, 47, 48, 57 and 59-60 under 35 U.S.C. § 103(a) as being obvious over Luyten in view of WO 95/16035 ("Celeste") and Cui et al., "Repair of thyroid cartilage defect with bone morphogenetic protein," Annals of Otology, Rhinology and Laryngology, 106, pp. 326-328 (1997) ("Cui"). The Examiner states that Luyten discloses CDMP-1 and CDMP-2 having *in vivo* chondrogenic activity in combination with a matrix for the repair of cartilage. The

Examiner also states that Luyten teaches that CDMPs can be combined with a number of suitable carriers such as fibrin glue, cartilage grafts and collagen and that the formulation can be administered via an injection. The Examiner states that Celeste teaches pharmaceutically acceptable carriers such as collagen, PLA, polymers of lactic acid, PGA and carboxymethylcellulose and that BMPs are useful in treating tendon or ligament defects as well as the formation of bone, cartilage, and tendon. The Examiner further states that Cui teaches the repair of thyroid cartilage defect with BMP by administering BMP for the replacement of lost laryngotracheal cartilage which results in new bone formation. The Examiner also states that Cui teaches that the ideal way to repair laryngotracheal defect is by inducing replacement cartilage growth. The Examiner, therefore, concludes that it would have been obvious to one skilled in the art to arrive at the claimed invention by combining the teachings of the cited references because all the references teach BMPs for inducing replacement growth of defects in cartilaginous tissues.

Applicants have amended claims 1 and 47 (and therefore, claims dependent thereon) to recite a method for repairing a defect locus in a nonarticular cartilage tissue and a method for promoting chondrogenesis at a nonarticular defect locus, respectively, using an osteogenic protein selected from the group consisting of OP-1, OP-2, OP-3, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-9, BMP-10, BMP-11, BMP-15, BMP-3B, DPP, Vg-1, Vgr-1, 60A protein, GDF-1, GDF-2, GDF-3, GDF-8, GDF-9, GDF-10 and GDF-11.

Luyten discloses the use of CDMP-1 and CDMP-2 in the therapeutic induction and maintenance of cartilage. Luyten, however, does not teach or suggest that any of OP-1, OP-2, OP-3, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-9, BMP-10, BMP-11, BMP-15, BMP-3B, DPP, Vg-1, Vgr-1, 60A protein, GDF-1, GDF-2, GDF-3, GDF-8, GDF-9, GDF-10 or GDF-11 are effective for repairing nonarticular cartilage tissue by inducing the formation of functional cartilage tissue or for promoting chondrogenesis at a nonarticular defect locus by inducing the formation of functional cartilage tissue, as recited in the amended claims. Neither



Celeste nor Cui remedies this deficiency. Celeste discloses that BMP-12 (also referred to as GDF-7 or CDMP-3) and BMP-13 (also referred to as GDF-6 or CDMP-2), either alone or in combination with other BMPs, induce tendon/ligament-like tissue healing and repair. Celeste does not teach or suggest that the specific osteogenic proteins recited in the amended claims may be used to repair nonarticular cartilage or promote chondrogenesis at a nonarticular defect locus by inducing the formation of functional cartilage tissue. Unlike the amended claims of the instant application, which require the formation of functional cartilage formation, Cui teaches that bovine BMP repairs a thyroid cartilage defect by inducing new bone formation which fills the defect in the cartilage. Therefore, nothing in Cui teaches or suggests that the specific proteins recited in the amended claims induce or promote functional replacement cartilage tissue.

Accordingly, nothing in the combination of Luyten, Celeste or Cui, teaches a method for repairing nonarticular cartilage tissue or a method of promoting chondrogenesis at a nonarticular defect locus by inducing functional cartilage

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tissue, as recited in the amended claims. Accordingly, applicants request that the Examiner withdraw this obviousness rejection.

Claims 1-6, 8-25, 27 and 30-34

The Examiner has rejected claims 1-6, 8-25, 27 and 30-34 under 35 U.S.C. § 103(a) as being obvious over Cui in view of Celeste. The Examiner states that Cui teaches the repair of thyroid cartilage defect by administering bBMP for the replacement of lost laryngotracheal cartilage which results in new bone formation. The Examiner also states that Cui teaches that the ideal way to repair laryngotracheal defect is by inducing replacement cartilage growth. The Examiner states that Celeste teaches that BMPs are useful in treating tendon or ligament defects as well as the formation of bone, cartilage, and tendon. The Examiner also states that Celeste teaches pharmaceutically acceptable carriers such as collagen, PLA, polymers of lactic acid, PGA and carboxymethylcellulose. The Examiner, therefore, concludes that it would have been obvious to one skilled in the art to arrive at the claimed invention by

combining the teachings of the cited references because both references teach BMPs for inducing replacement growth of defects in cartilaginous tissues.

As described above, applicants have amended claim 1 (and therefore, claims dependent thereon) to recite a method for repairing a defect locus in a nonarticular cartilage tissue using an osteogenic protein selected from the group consisting of OP-1, OP-2, OP-3, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-9, BMP-10, BMP-11, BMP-15, BMP-3B, DPP, Vg-1, Vgr-1, 60A protein, GDF-1, GDF-2, GDF-3, GDF-8, GDF-9, GDF-10 or GDF-11, wherein the method induces the formation of functional replacement cartilage tissue.

Although Cui discloses that the ideal method for replacing laryngotracheal cartilage would be to induce replacement cartilage, it nevertheless teaches that bovine BMP repairs a thyroid cartilage defect by inducing new bone, not cartilage. Nor does Celeste provide any teaching or suggestion that the recited osteogenic proteins claimed in the instant application are capable of inducing replacement cartilage tissue. Celeste discloses that BMP-12 (GDF-7) and BMP-13 (GDF-6), either

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alone or in combination with other BMPs, induce tendon/ligament-like tissue healing and repair. Celeste does not teach or suggest that the specific osteogenic proteins recited in the amended claims may be used to repair a defect locus in a nonarticular cartilage tissue, thereby inducing the formation of functional replacement cartilage tissue to repair the defect locus.

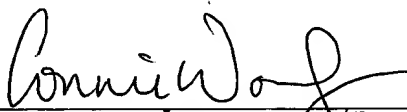
Thus, nothing in the combination of Cui or Celeste, teaches a method for repairing a defect locus in a nonarticular cartilage tissue, thereby inducing the formation of functional replacement cartilage tissue to repair the defect, using the specific osteogenic proteins recited in the amended claims. Accordingly, applicants request that the Examiner withdraw this obviousness rejection.

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CONCLUSION

In view of the foregoing remarks and amendments, applicants request that the Examiner favorably reconsider this application and allow the claims pending herein. If the Examiner believes that a telephone conference would expedite allowance of this application, she is invited to telephone the undersigned at any time.

Respectfully submitted,



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